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Editorial: Of Floors and Ceilings—Defining, Assuring, and Communicating Vaccine Safety

In an era when, as a result of technological marvels, we have gone to the moon, our machines are on Mars, we have same-day transportation to nearly anywhere on Earth, and information (although not necessarily accurate) can be offered instantly to millions of people by way of computers, one of our greatest achievements has been the development and use of immunizations. By sustaining health, preventing suffering, and averting death, immunizations make other achievements possible.

In our lifetime, public health vaccination programs have eradicated smallpox. They are reducing paralytic polio to a dot on the horizon of the past; its eradication in the near future is a realistic hope. *Haemophilus influenzae* type B disease, once the leading cause of fatal meningitis, has dwindled dramatically in developed countries in the decade since vaccines against this disease were introduced. Many other devastating diseases are now on the ropes as a result of immunizations.

No technological feat is without cost, and no medical procedure is entirely free of risk. For that matter, life itself is riddled with risks, among them illness, suffering, disability, and death from disease. A few decades ago, the magnitude of risk from disease was apparent to all. As immunization programs have resulted in sustained, unprecedented low rates of vaccine-preventable diseases, however, perceptions of disease risks have faded. Some have turned their focus to the risks of vaccination. With the pace of high-tech communication far surpassing the necessarily plodding steps of data gathering and analysis, public health workers are encountering questions about vaccine safety. Some of these questions stem from reports

of a single or exceedingly rare adverse event that is linked only anecdotally to vaccination. Even when an adverse event is clearly unrelated to vaccination, it is currently difficult, if not impossible, to inform and reassure the public.

In this issue, Tuttle and coauthors analyze data from existing surveillance systems for an association between tetanus-toxoid-containing vaccines and Guillain-Barré syndrome.¹ If an association exists, they conclude, it must be minuscule. These results conflict with an earlier report from the Institute of Medicine, which suggested, while acknowledging limitations in data, that an association is possible.² Tuttle et al. note with 95% confidence that the relative risk of persons' developing Guillain-Barré syndrome after receiving tetanus-toxoid-containing vaccines is between .09 and 3.32 times that of unvaccinated persons. However, as the authors acknowledge, their conclusions are limited by sample size, and a far more expensive study would be needed to narrow the confidence intervals.¹

Given a baseline rate of Guillain-Barré syndrome of 1.45 cases per 100 000 persons per year,¹ we might well ask, How critical is it to narrow that confidence interval? While the findings of Tuttle et al. are reassuring, what level of risk are we willing to live with when it comes to immunizations? Logically, tolerable risk depends upon perceived threat of the disease, the nature of the risk of immunization, and the outlook of the person (or parent) taking the risk. However, one person's floor is another person's ceiling. What to one is an acceptable risk, given the benefit, to another may be unacceptable.

Lives hang in the balance. In countries where vaccination levels have fallen, epi-

demics of vaccine-preventable diseases have followed; for example, witness the reemergence of pertussis in several European countries^{3,4} and Japan⁵ when pertussis vaccines were removed from nationwide immunization programs.

Both the benefits and the risks of immunization must be measured with societal yardsticks as well as thorough epidemiological work. The continued success of childhood immunization programs rests on the public's trust. We must honor that trust by maintaining our diligence in monitoring vaccine lots and responding to adverse events. Messages to parents must be comprehensible and trustworthy, enabling parents to have confidence that existing vaccines are safe, that whatever risk exists is negligible, and that the risk is far outweighed by the personal and societal benefits.

By all accounts, most parents do believe these things. But trust is often fragile. In the late 1950s, the public's trust was strained when 260 cases of poliomyelitis were linked with polio vaccine. Once it was clear that all cases were linked to one manufacturer (Cutter), the Public Health Service immediately suspended vaccination, recalled the Cutter vaccine, and launched an intensive, wide-reaching investigation.⁶ The resumption of the vaccination program was well accepted by the public,⁶ perhaps because of the stamina of the scientifically sound response. Tuttle and colleagues provide a glimpse of the type of credible scientific work needed to ensure that support for immunization programs is maintained,

Editor's Note. See related article by Tuttle et al. (p 2045) in this issue.

even as epidemics of deadly vaccine-preventable diseases become history and recollections of their impact become more remote.

We are just in the beginning stages of what is possible with vaccines. The number of newly licensed vaccines and those in the pipeline, including rotavirus, Lyme disease, and conjugate pneumococcal vaccines,⁷ is accelerating. Recent biomedical advances will expedite the development of safe and effective vaccines against a variety of diseases that continue unabated globally, including tuberculosis, acquired immunodeficiency syndrome (AIDS), and malaria.⁸ Each success will result in questions of risk; therefore, the sciences of vaccine safety and risk communication must be tackled in a sustained and comprehensive way.

Tuttle and coauthors question whether additional precious resources should be allotted to more precisely defining the risk of Guillain-Barré syndrome following immunization with tetanus-toxoid-containing vaccines. To be cost-effective, as recommended by the National Vaccine Advisory Committee, we need sufficiently large, geographically and socioeconomically representative, population-based surveillance systems for vaccine-associated adverse events, and these surveillance systems should have stable, long-term support.⁹ Such systems will make it possible to answer a myriad of specific questions (like this one) to accurately determine causality and define incidence for a variety of vaccine-specific events.

We must ensure that our regulatory system has sufficient resources to continue, in partnership with vaccine companies, to make certain that vaccines are free of adventitious or other contaminating agents, particularly as the number of vaccine products increases.

Finally, we need better information on how the public processes information on vaccine-associated risks and benefits. Then we can communicate what we know in a way that will be heard and understood, so

that parents will be confident about the need for and safety of immunizations. Although they are vital to communication among investigators, phrases such as "minimal risk" and "not of significant public health importance" may actually distance the data from the people who need to know their meaning. The art of risk communication, well developed in the areas of environment, cancer, and transportation safety, is in its infancy for immunization programs.¹⁰ Because vaccines are actively promoted and given to healthy babies to prevent diseases that may not strike a specific child, uniquely challenging issues of risk communication are raised.

Vaccines are our greatest tools for use in combating illness and complications from infectious diseases. We must never let our guard down against those diseases for which we now have vaccines. We must continue to strive to develop new, safe, and effective means to prevent diseases for which vaccines are currently not available. Essential to an effective vaccine program is a systematic approach to producing safe vaccines, quickly recognizing and defining unexpected adverse events, and effectively informing the public with credible, precise information about benefits and risks. As in all scientific investigation, we should unhesitatingly take, in Henry James' words in "Fordham Castle," "a straight and possibly dangerous dive into the very depth of truth." It is clearly worth the risk. □

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